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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

ROARK, JESSICA H

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/380,579

Applicant(s)

IKEHARA ET AL.

Examiner

Jessica H. Roark

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jessica Roark, Art Unit 1644, Technology 1600.

2. Applicant's after final amendment, filed 1/16/02 (Paper No. 16), has been entered.
Claim 10 has been amended.
Claims 1-8 have been canceled previously.
Claims 9-12 have been added previously.

Claims 9-12 are pending and under consideration in the instant application.

3. After further consideration, the finality of the rejection of the last Office Action is withdrawn.
An Action on the Merits follows.

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed*.

6. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

In addition, the use of "novel" in the abstract should be avoided as patents are presumed to be novel and unobvious.

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7. The formal drawings submitted 9/7/99 have been approved by the Draftsman.
8. Applicant's IDSs, filed 10/12/99, 12/9/99 and 5/3/00 (Paper Nos. 3-5), are again acknowledged.
9. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.
10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
11. Applicant's amendment, filed 1/16/02, has overcome the previous rejection of claim 10 under 35 USC 112, first paragraph, as lacking an adequate written description.
12. After further consideration, the previous rejection of claims 9-12 under 35 USC 112, first paragraph for lack of enablement is withdrawn.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "immunological tolerance" is indefinite in that the metes and bounds of the phrase to do not appear to be established by the specification or claims.

It is suggested that Applicant either identify a definition of the metes and bounds of this phrase that is supported in the specification as filed; or alternatively amend the claims to recite definite language that is supported by the specification.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

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15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Ildstad (US Pat. No. 5,514,364, see entire document).

Ildstad teaches and claims a method of conditioning of a recipient intended for organ grafting by subjecting the recipient to sublethal total body irradiation and administering to the recipient whole bone marrow (see entire document, but especially the claims and columns 5, 8, 17 and 21-22).

Ildstad also teaches that bone marrow engraftment after sublethal total body irradiation is reliably achieved in 100% of recipients at 7 Gy (see Figure 1 and column 17, especially lines 4-25).

Ildstad further teaches transplantation of organs to the bone marrow recipient and exemplifies skin transplantation, showing that the recipients are specifically tolerant of the donor-type skin (see e.g., Abstract and columns 21-22).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitation of "tolerogen effective" would be an inherent property of the dose of bone marrow cells administered; and the preamble requiring "inducing immunological tolerance" would be achieved by the referenced method steps, particularly since the metes and bounds of this phrase are indefinite as noted supra and in view of the skin graft tolerance taught by Ildstad.

In addition, although a route of administration of the bone marrow is not stated by Ildstad, intravenous administration would have been inherently used in the method taught since the intravenous route was the art recognized and standard mode of bone marrow administration.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

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18. Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ildstad (US Pat. No. 5,514,364) in view of Zhang et al. (Eur. J. Immunol. 24 :1558-1565, IDS).

The claims are drawn to a method comprising administering to an organ transplant recipient total body sublethal irradiation of at least 6.5 Gy or 6.5 Gy to 7.0 Gy; and administering whole bone marrow cells either intravenously or by hepatic portal administration; the method optionally further comprising transplanting the organ within the same day as the bone marrow administration.

Ildstad teaches and claims a method of conditioning a recipient intended for organ grafting by subjecting the recipient to sublethal total body irradiation and administering to the recipient whole bone marrow (see entire document, but especially the claims and columns 5, 8, 17 and 21-22).

Ildstad also teaches that bone marrow engraftment after sublethal total body irradiation is reliably achieved in 100% of recipients at 7 Gy (see Figure 1 and column 17, especially lines 4-25).

Ildstad further teaches transplantation of organs to the bone marrow recipient and exemplifies skin transplantation, showing that the recipients are specifically tolerant of the donor-type skin (see e.g., Abstract and columns 21-22).

Ildstad does not teach hepatic portal vein administration of the whole bone marrow, nor does she teach transplanting an organ within the same day as administration of the bone marrow.

However, Zhang et al. teach that in both intravenous and portal vein injections of bone marrow cells (BMC), most of the cells migrate to the liver, although more BMC do so after portal vein administration than after intravenous administration (see entire document, especially Figures 3 and 5 and page 1563 at the 4th full paragraph).

Zhang et al. also review the art recognized prolongation of organ graft survival in a recipient when cells from the donor are administered to the recipient via the portal vein in addition to the transplanted organ, and note that this is due to a form of immunological tolerance (see especially the "Introduction" on page 1558 and the 1st paragraph of "Discussion" on page 1563).

Given the teachings of Zhang et al. that prolonged organ graft survival was known to be achieved when donor cells were also administered via the hepatic portal vein, one of ordinary skill in the art would have found it obvious to modify the teachings of Ildstad to administer the bone marrow cells by hepatic portal venous administration. One of ordinary skill in the art at the time the invention was made would have been motivated to combine sublethal irradiation and administration of the bone marrow cells via the hepatic portal vein to provide an improved method for inducing immunological tolerance in an organ transplantation recipient. Given the teachings of Ildstad and Zhang et al., one of ordinary skill in the art would have reasonably expected that combining two art-recognized approaches for inducing immunological tolerance would have also resulted in a method of inducing immunological tolerance in an organ transplantation recipient. Finally, given the art recognized time constraints associated with transplanting cells and organs from the same human donor; one of ordinary skill in the art would have also been motivated to transplant the organ within the same day as the whole bone marrow cells. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
January 28, 2002

PHILLIP GAMBEL, PH.D.
PRIMARY EXAMINER
TECH CENTER 1600
1/28/02